Pharmacokinetic Services

Evaluation of lead compounds in preclinical species is a prerequisite for the progression of drug candidates in the drug discovery and development process.

In vivo pharmacokinetic (PK) studies provide information on the changes in drug concentration with time, usually in blood or plasma, following dosing. Data from animal PK studies is used by medicinal chemists to optimize compounds and by pharmacologists to design, interpret efficacy and toxicology studies, and link the observed PD effect to the concentration (PK/PD), as well as to predict the PK profile in humans. Within the lead optimisation phase, the first PK studies are usually performed in rodents followed by non-rodents at later stages.

In addition to *in vivo* studies, at Fidelta we have the capability to ensure a range of services including bioanalytical method development, quantitative and qualitative analysis, vehicle assessment and stability testing, and pharmacokinetic calculations.

Fidelta provides both predesigned and customizable studies with rapid turnaround time and high quality.
These include:

- **Exploratory/Rapid PK**

  Basic PK parameters, Blood/Plasma sampling, Cassette Dosing

- **Full PK profiling:**

  Bioavailability, Dose proportionality, Tissue distribution, Brain-to-plasma ratio, Bioequivalence, Single vs. multiple dosing, Metabolite profiling

Administration routes and sampling

Dosing routes:

oral, intravenous (bolus and infusion), subcutaneous, intramuscular, intraperitoneal, intratracheal, intranasal, and intraduodenal

Sample collection:

Serial sampling: tail or saphenous vein; sampling from catheter

Terminal sampling: cardiac puncture or arterial/vein sampling

Matrices:

A variety of matrices can be collected:

- Blood/plasma/serum
- Tissues (e.g. liver, lung, brain, muscle, etc.)
- Urine/faeces collection in metabolic cages.

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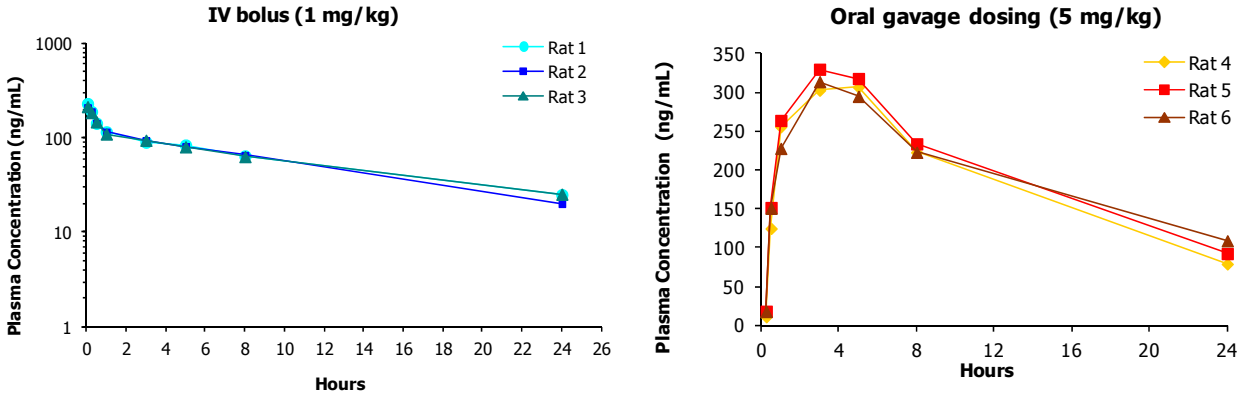
Pharmacokinetic Services

Example of a full PK study design to assess bioavailability in rat	
Animal Weight	Rat: 180-250g
Routes	i.v. bolus and oral gavage (p.o.)
Dose and dosing volume	i.v. (1 mg/kg administered at 5 mL/kg); p.o. (2 or 5 mg/kg administered at 10 mL/kg)
Food	i.v.: ad libitum; p.o.: fasted up to 4 hr following administration
Number of animals	Serial sampling: n=3/route
Sampling site	Tail-vein (serial)
Samples	Blood samples are collected in anticoagulant coated polypropylene tubes and kept on ice. Either blood or plasma is frozen following collection and analyzed for test compound concentration.
Time points (h)	i.v.: 0.08- 0.25- 0.5- 1- 2- 4- 8- 24; p.o.: 0.25- 0.5- 1- 1.5- 2- 4- 8- 24
Sample Preparation/ Bioanalysis	Samples and formulation aliquots are processed using an appropriate extraction procedure (e.g. protein precipitation) and analysed using a previously established LC-MSMS method.
PK parameters	CL, V_{ss}, $t_{1/2}$, C_{max}, T_{max}, AUC $_{(0\text{-}t)}$, AUC $_{(0\text{-}inf)}$, F



Figures 1 & 2. Plasma concentration of a test compound following i.v. bolus and oral gavage administration in rat

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